AMENDMENTS TO THE CLAIMS

Please amend claims 1 and 9 and cancel claims 2 and 6 without prejudice or disclaimer and please add claims 96-98. The following listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently Amended) A method of selecting a multi-zinc-finger polypeptide that binds to a sequence of interest comprising at least two subsites, said method comprising the steps of:

   a) incubating position-sensitive primary libraries with target site constructs under low-stringency conditions sufficient to form first binding complexes, wherein said primary libraries comprise multi-zinc-finger polypeptides having one variable finger and at least one anchor finger, and wherein the target site construct has one subsite with a sequence identical to a subsite of the sequence of interest, and one or more subsites with sequences to which the anchor finger(s) bind; ~~with low affinity;~~

   b) isolating pools comprising nucleic acid sequences encoding the multi-zinc-finger polypeptides having one variable finger that formed ~~in the~~ first binding complexes ~~of step a)~~ with the target site constructs in step a);

   c) recombining the nucleic acid sequences encoding the ~~one~~ variable ~~finger~~ fingers from the isolated pools of step b) to produce a secondary library encoding multi-zinc-finger polypeptides having zinc-fingers partially optimized for binding to subsites ~~of~~ that together comprise the sequence of interest;

   d) incubating the secondary library of step c) with the sequence of interest under high-stringency conditions sufficient to form second high-affinity binding complexes between the multi-zinc-finger polypeptides and the sequence of

interest, wherein the high-stringency conditions are more stringent than the low-stringency conditions in step a); and

e) isolating nucleic acid sequences encoding multi-zinc-finger polypeptides that formed in the second binding complexes of step d).

2. (Previously Presented) The method of claim 1, wherein the multi-zinc-finger polypeptide comprises at least two zinc-fingers.

3. (Previously Presented) The method of claim 2, wherein the multi-zinc-finger polypeptide comprises three or more zinc-fingers.

4. (Original) The method of claim 1, wherein the target site construct comprises the same number of base pairs as the sequence of interest.

5. (Original) The method of claim 1, wherein a subsite comprises 2-5 base pairs.

6. (Original) The method of claim 1, wherein the target site construct comprises two or more subsites.

7. (Original) The method of claim 1, wherein the target site construct comprises three or more subsites.

8. (Cancelled)

9. (Currently Amended) The method of ~~claim 8,~~ claim 1, wherein ~~the remaining subsite(s) have sequences~~ at least one of the one or more subsites with sequences to which the anchor finger(s) bind has a sequence selected from the group consisting of SEQ ID NO. 5 (GCC subsite 1), SEQ ID NO. 6 (GAA subsite 2) and SEQ ID NO. 7 (GCA subsite 3).

10. (Previously Presented) The method of claim 1, wherein the primary libraries comprise polypeptides having at least one anchor finger that is derived from a naturally occurring zinc-finger polypeptide.

11. (Cancelled)

12. (Previously Presented) The method of claim 10, wherein the zinc-finger polypeptide is selected from the group consisting of Zif268, tramtrack, GLI, YYI and TFIIIA.

13. (Previously Presented) The method of claim 12, wherein the zinc-finger polypeptide is Zif268.

14. (Previously Presented) The method of claim 1, wherein the primary libraries comprise polypeptides having at least one anchor finger that is derived from a synthetic derivative of Zif268.

15. (Previously Presented) The method of claim 14, wherein the derivative of Zif268 comprises sequences selected from the group consisting of SEQ ID NO:2 (DRSSLTR, finger 1), SEQ ID NO:3 (QGGNLVR, finger 2) and SEQ ID NO:4 (QAATLQR, finger 3).

16. (Previously Presented) The method of claim 1, wherein the variable finger is derived from a naturally occurring zinc-finger polypeptide.

17. (Previously Presented) The method of claim 16, wherein the zinc-finger polypeptide is selected from the group consisting of Zif268, tramtrack, YYI, GLI and TFIIIA.

18. (Original) The method of claim 17, wherein the zinc-finger polypeptide is Zif268.

19. (Previously Presented) The method of claim 1, wherein the variable finger is derived from a synthetic derivative of Zif268.

20. (Previously Presented) The method of claim 19, wherein the synthetic derivative of Zif268 comprises sequences selected from the group consisting of SEQ ID NO:2 (DRSSLTR, finger 1), SEQ ID NO:3 (QGGNLVR, finger 2) and SEQ ID NO:4 (QAATLQR, finger 3) and combinations thereof.

21. (Previously Presented) The method of claim 1, wherein the variable finger comprises six randomized amino acid residue positions located within, or just amino-terminal to the start of, the recognition alpha helix of the variable finger.

22. (Previously Presented) The method of claim 21, wherein the randomized amino acid residue positions are -1, +1, +2, +3, +5 and +6, numbered with respect to the start of the recognition alpha helix of the variable finger.

23. (Original) The method of claim 21, wherein between 16 to 20 amino acids are represented at each randomized position.

24. (Original) The method of claim 21, wherein between 16 to 19 amino acids are represented at each randomized residue position.

25. (Original) The method of claim 21, wherein 16 amino acids are represented at each randomized residue position.

26. (Original) The method of claim 1, wherein the primary libraries are expressed in vitro.

27. (Original) The method of claim 1, wherein the primary libraries are expressed in expression systems selected from the group consisting of eukaryotic, prokaryotic and viral expression systems.

28. (Original) The method of claim 27, wherein the primary libraries are expressed in bacteria.

29. (Original) The method of claim 1, wherein incubation of the primary libraries is performed in vitro.

30. (Original) The method of claim 1, wherein incubation of the primary libraries is performed within a prokaryotic or eukaryotic cell.

31. (Original) The method of claim 30, wherein the incubation is performed within a bacterial cell.

32. (Original) The method of claim 1, wherein the isolated pools of nucleic acid sequences are recombined to produce a secondary library by PCR-mediated recombination.

33. (Original) The method of claim 1, wherein the secondary library is expressed in vitro.

34. (Original) The method of claim 1, wherein the secondary library is expressed in an expression system selected from the group consisting of a eukaryotic, prokaryotic and viral expression system.

35. (Original) The method of claim 34, wherein the secondary library is expressed in bacteria.

36. (Cancelled)

37. (Original) The method of claim 1, wherein incubation of the secondary library is performed in vitro.

38. (Original) The method of claim 1, wherein incubation of the secondary library is performed within a prokaryotic or eukaryotic cell.

39. (Original) The method of claim 38, wherein the incubation of the secondary library is performed within a bacterial cell.

40.– 95. (Cancelled)

96. (New) The method of claim 1, wherein the method does not utilize a polysome system.

97. (New) The method of claim 1, wherein the high-stringency conditions comprise one or more of a lower salt concentration than the low-stringency conditions, a temperature of 65 ℃ or greater, and detergent at a concentration of about 0.1% to about 2%.

98. (New) The method of claim 1, wherein incubation of the first and/or second library is performed within a prokaryotic or eukaryotic cell, and the low- and/or high-stringency condition is a growth condition.